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Resection of tumors within and near to the primary Sensory-Motor cortex using Phase reversal Cortical mapping and bipolar stimulation

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***Abstract*---**Objective Brain mapping techniques allow one to effectively approach tumors involving the primary sensory-motor cortex and nearby area (M1). Tumor resectability and maintenance of patient integrity depend on the ability to successfully identify motor tracts during resection by choosing the most appropriate neurophysiological paradigm for motor mapping. Mapping with a high frequency (HF) stimulation technique has emerged as the most efficient tool to identify motor tracts because of its versatility in different clinical settings. At present, few data are available on the use of HF for removal of tumors predominantly involving M1. Methods The authors have analysed a series of 6 patients with brain tumors within M1, by reviewing the use of HF as a guide. The neurophysiological protocols adopted during resections were described and correlated with patients' clinical and tumor imaging features. Feasibility of mapping, extent of resection, and motor function assessment were used to evaluate the oncological and functional outcome to be correlated with the selected neurophysiological parameters used for guiding resection. The study aimed to define the most efficient protocol to guide resection for each clinical condition. Results The data confirmed HF as an efficient tool for guiding resection of M1 tumors, 90% complete resection and only 2% permanent morbidity. HF was highly versatile, adapting the stimulation paradigm and the probe to the clinical context. Standard approach of stimulation and cortical surface electrode strip with 4 sensors were used. Conclusions

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Resection of M1 tumors is feasible and safe. By adapting the cortical mapping and bipolar stimulation to motor cortex, the best resection and functional results can be achieved.

Keywords---gliomas, clinical outcome, intraoperative mapping, neurophysiology, functional balance, extent of resection, morbidity, deficit, oncology.

Abbreviations

M1= primary sensory-motor cortex and near by region; AED = antiepileptic drug; cMT = cortical motor threshold; DWI = diffusion-weighted imaging; ECoG = electrocorticography; EEG = electroencephalography; EMG = electromyography; EOR = extent of resection; HF = high frequency; HGG = high-grade glioma; LGG = low-grade glioma; MEP = motor-evoked potential; MRC = Medical Research Council; MT = motor threshold; sMT = subcortical motor threshold

Introduction

Resection of tumor in primary motor cortex (M1) is usually considered a surgical off-limits area due to its essential role in motor function.[6,10] It requires the identification of critical motor sites during surgery to maximize tumor resection while maintaining the patient's functional motor integrity.[2,12,15] In this regard, the use of intraoperative neurophysiology is the most efficient tool currently available as it provides real-time intraoperative feedback to surgeon and offers different stimulation paradigms and probes to be able to locate key motor sites during tumor removal.[3,11]

Despite these advances, resection of tumors harboured primarily in M1 is still highly challenging. M1 is particularly vulnerable to surgical insults. Damage to M1 is usually associated with the occurrence of permanent motor deficits, with limited ability to subsequently recover.[6] This has historically constrained the surgical approach for M1 tumors to a simple biopsy, eliminating more widespread tumor removal because of consistent and unacceptable long-term morbidity.[4] Data on surgical treatment of M1 tumors are thus very limited. Some reports are available on limited series or anecdotal cases, mainly involving well-demarcated tumors,[9] in which traditionally available mapping paradigms are, to a certain extent, quite efficient. Studies in larger series on different tumor types reported variable extent of resection (EOR) and postoperative permanent morbidity.[5,8,13,14] More recently, evidence that the assistance of a brain mapping technique applied to M1 tumors affords an excellent resection suggests that these tumors are indeed amenable to resection and should not be labelled unresectable.[1,7] Resectability and maintenance of patient integrity depend on the ability to successfully identify motor tracts during resection.[5] In this regard, the choice of the most appropriate neurophysiological protocol to perform motor mapping is critical[1].Ideally, the best neurophysiological paradigm should be highly feasible in the operating room, should work in all clinical conditions, and should be associated with the lowest percentage of false-negative or false-positive results. Various paradigms or probes are currently available for motor mapping, and their properties, clinical use, and pitfalls have been described.[16,17]

In a previous study reviewing the use of available neurophysiological protocols for guiding resection of tumors involving motor pathways, high-frequency (HF) stimulation (pulse technique) emerged as the most efficient tool to stimulate the motor pathways because of its flexibility of use in different clinical settings, allowing a high percentage of resection and a low rate of deficits.[1] However, few data are available on the use of HF stimulation for removal of tumors predominantly involving M1. We have routinely submitted patients harbouring tumors within M1 to surgery, moving toward the idea that resection can be performed efficiently and that it is beneficial for both oncological and functional reasons. In all cases, HF stimulation was used as a guide for performing both cortical and subcortical mapping. In this study we analysed 6 cases of prospective patients with brain tumors admitted between 1st April 2022 to October 2022, whose tumor mass was found near or within sensory-motor area (M1), and critically reviewed with use of electrophysiological mapping of sensory-motor cortex and with the use of HF stimulation as a guide. The neurophysiological mapping protocols and/or probes adopted were described and correlated with patients' clinical features or tumor imaging characteristics. The aim was to remove maximum tumor with preserving best motor and sensory function of patient.

Methods

Patients

We reviewed patients admitted to our hospital at Sumandeep medical college , between 1st April 2022 to October 2022. We have included patients with the tumor mass located within sensory-motor cortex- M1. All patients provided informed consent for the procedure, covered by our Ethical Committee.

Imaging

The preoperative MRI protocol, acquired , included 1) axial 3D FLAIR imaging; 2) post-Gd 3D T1-weighted imaging; and 3) diffusion-weighted imaging (DWI) and apparent diffusion coefficient DWI. Patients postoperative MRI (volumetric FLAIR and post-Gd T1-weighted) to estimate EOR.[18] Immediate postoperative diffusion-weighted MRI scans were performed to evaluate ischemia.

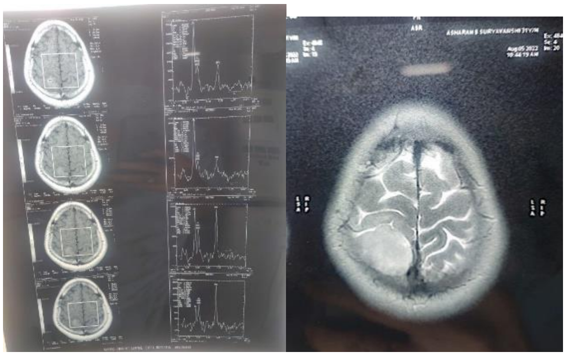

Fig 1. Pre-operative MRI Right Fronto-parietal tumor Near M1 area

Surgical Procedure

The aim of resection was a complete resection when feasible, according to functional boundaries. With the aid of pre-operative CT scan and MRI, a craniotomy tailored to expose the cortex corresponding to the tumor area and a limited amount of surrounding tissue was performed. Cortical mapping was performed to define the cortical safe-entry zone. Cortical brain stimulation was performed to map the tumor periphery to locate functional boundaries since the initiation of the resection. The mass was finally removed only when subcortical tracts were identified and the tumor was functionally disconnected. For pure Rolandic tumors, the peripheral functional motor borders were initially located all around the tumor, and then the tumor mass was removed. In cases of tumors extending anteriorly or posteriorly, subcortical functional tumor disconnection was started at the M1 level and continued anteriorly (in pre-M1 tumors) or posteriorly (in post-M1 tumors).

Neurophysiological Protocols

The intraoperative neurophysiology protocol used to guide resection consisted of brain monitoring and mapping tools.

Modalities used

- MEPs (Motor Evoked Potential)
- Central Sulcus Mapping (CSM) Phase Reversal – For Motor & Sensory Cortex Mapping
- Cortical Mapping – To Map Motor Areas
- Sub Cortical Mapping – For Corticospinal Tracts distance from the tumor (CST)

Brain Monitoring

Electroencephalography (EEG) and electrocorticography (ECoG) were continuously monitored to assess the depth of anaesthesia and occurrence of seizures/after discharges. Free-running electromyography (EMG) activity was monitored from the beginning with a multichannel recording setup; as many as 12 muscles were recorded from different contralateral and ipsilateral muscles.

The recording system was aimed at monitoring the following during surgery: 1) free-running background EMG activity; 2) motor responses to brain mapping stimulation; and 3) motor-evoked potentials (MEPs) evoked by stimulation of M1 using the "train of 5" (To5) technique throughout the procedure to monitor the integrity of descending motor pathways. MEPs were recorded from transcranial electrodes from incision to closure, and from strip electrodes during the resection period (from dura opening to dura closure).[3] Small 4-contact strips were placed very close to the surgical field (Fig.2)

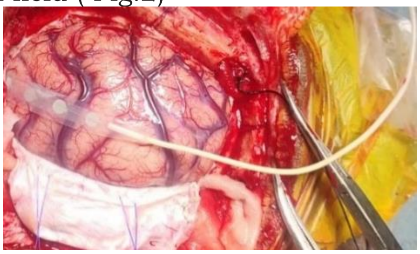

Fig 2. Cortical surface elecrode strip with 4 sensors.

While recording responses from 4 point strip application on cortical surface of sensory and motor cortex, we can see phase reversal pattern as show in fig 3.

Fig 3.

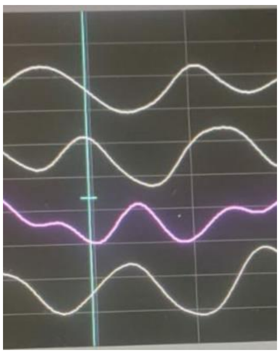

Fig 4

As shown in Fig 3 upper wave is from sensory cortex and lower wave is from motor cortex. You can see reverse pattern of recorded wave from motor cortex compared to the wave of sensory cortex. In Fig-4, you can find that upper 2 waves are from sensory cortex and it's phase reverse pattern is seen in lower two waves , these 4 waves are recorded from 4 point set of sensors applied on cortical surface of brain in operative field.(Fig-2). Real time view of waves recorded are shown in Fig-5.

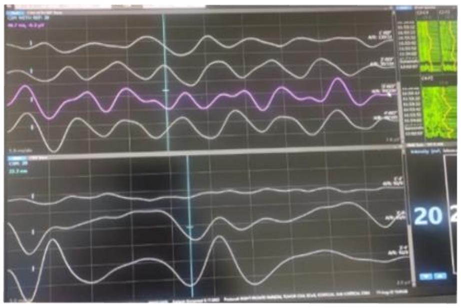

Fig 5. Screen showing recorded waves intra-operatively.

Occasionally, cortical MEPs were also recorded during resection by direct cortical stimulation to warrant corticofugal fibre integrity. Both contralateral and ipsilateral orofacial as well as upper and lower limb muscle responses were recorded.[3]

Brain Mapping

Mapping techniques were used to perform cortical mapping and to locate functional boundaries subcortically. HF constant-current stimulation was adopted. Stimulation paradigms consisted of a short train of stimuli, with 50-60Hz, variable pulse duration (1000 μsec), bipolar probe and biphasic stimulation for duration of 4 seconds. Current was used is 1 mA to 20 mA. current intensity was not increased above 25 mA. For cortical mapping, when a stable motor response was obtained, the intensity of cortical stimulation (mA) was progressively decreased to threshold (cortical motor threshold [cMT]) in order to find the motor hotspot. Hence, a strip electrode was placed for MEP monitoring. For subcortical mapping, intensity of stimulation was used to appreciate distance from the corticofugal pathways, and progressively decreased to threshold (subcortical motor threshold [sMT]) to define the margins of resection.

Factors Considered for Analysis

Demographic and clinical features at admission included age, sex, clinical history and presenting symptoms, previous treatments, type and number of seizures and seizure control, and current and previous drug uptake. Neurological assessment was performed at admission, at 1 week after surgery, and at a 1-month follow-up. Motor conditions were categorized using the Medical Research Council(MRC) scale evaluation, and requirement for rehabilitation was recorded. Tumor imaging variables were deducible from conventional preoperative MRI and included volume, zone location, side, border, presence of contrast enhancement, outcrop of the M1 cortex, and extension outside the M1 cortex. The contrast-enhancing portion of the tumor (the target of resection) was measured. For low-grade, non–contrast-enhancing tumors, the FLAIR signal (the target of resection) was used.

To evaluate tumor location, M1 was divided into three motor zones (zone 1, lower limb; zone 2, upper limb; and zone 3, face), as previously reported.[9] Tumor borders were defined as well defined or irregular,[12] using postcontrast imaging for contrast lesions, or FLAIR images for those that were nonenhancing. Outcropping of M1 was defined as present when the tumor was reaching the cortex, either on coronal and/or sagittal FLAIR images for nonenhancing lesions, or on T1-weighted postcontrast images for enhancing lesions. Regarding the extension of the tumor in cases of large tumor volume, the tumor could extend anteriorly toward the dorsal premotor cortex or the supplementary motor cortex or posteriorly toward the primary sensory cortex. The extension was categorized accordingly.

Results

Patients

Six patients with a tumor principally in volving M1 were treated surgically. Clinical and imaging features are reported in Table 1. Most patients experienced seizures, requiring at least 1 antiepileptic drug (AED) to be controlled.

Surgical Data and EOR(extent of resection)

Surgery was always performed under general anaesthesia and near total resection done in all cases. EEG and ECOG were used to monitor the level of anaesthesia, titrated to obtain continuous EEG and ECOG activity, avoiding any burst suppression. Cortical and sub cortical motor mapping was always performed using HF stimulation. Cortical motor mapping was used to define the safe cortical entry zone, identified in all cases; sub cortical motor mapping defined the functional boundaries and margins of resection. MEP monitoring, recorded from strip electrodes during the entire resection procedure, showed no abnormalities.

Motor Functions

A decline of motor function was observed in 3 patients immediately after surgery(MRC grade 4(2) and MRC grade <4(1); Table 1),which completely recovered at follow up in all but 1 case. In the latter, the motor deficit was mild (MRC grade 4);this patient was operated on for HGG. No permanent deficits were registered in patients who underwent operations for LGGs. Rehabilitation was needed for 2 patients. Post op Praxia was seen in one patient.

Table 1

Clinical And Demographic Features	
Gender	
Male	4
Feamle	2
Age	
Mean	35 yr
Range	30 yr-45 yr
Focal seizures	

	4
Duration of clinical history	
>6 months	1
No of AED Pre-Op.	
1	4
>1	--
Pre-Op motor deficit	
	1
MRC grade	
5	5
4	1
Radiological And Surgical features	
Tumor side	
Right	4
Left	2
Contrast enhancement	
	3
Tumor extension	
Anterior	4
Posterior	2
Tumor border	
Irregular	3
Well defined	3
Cortical outcrop	
	4
Resection	
Total	4
Subtotal	2
Worsening of motor deficit post op	
	3
1st Wk MRC scale	
5	3
4	3
1 month MRC scale	
5	5
4	1
Post op Rehabilitation	
	1
Histology	
LGG	4
HGG	2
Others	--

Discussion

Recent data demonstrated that M1 tumors are amenable to resection with an acceptable low morbidity.[7] Resection feasibility is strongly associated with the use of a brain mapping technique.[3] We used cortical mapping and identification of motor cortex, which helped us to resect near total excision of tumor and it prevented us to injure motor cortex during tumor resection. Our data confirmed that resection of tumors principally involving M1 is feasible. The chance of achieving a complete resection was high (85.3%), particularly in cases of tumors with well-defined borders or contrast enhancement, independent of location or a patient's clinical features. However, a complete resection was also feasible in the large majority of irregular border tumors (lower grade), or in those with previous treatments. Although the rate of immediate postoperative deficits was high, as expected when functional boundaries are reached at the subcortical level, resection was associated with low permanent morbidity (2%). Permanent deficits were restricted to patients with HGG, confirming that HGGs are at major risk of morbidity.[7]

The standard HF approach was particularly efficient in patients with well-controlled seizures and harbouring tumors with well-defined borders or contrast enhancement, and generally reaching the surface. In this setting, the reliability of cortical mapping was high, allowing us to identify the safe-entry zone and, at a subcortical level, the functional motor boundaries at the lowest MT. A modification of the standard HF paradigm was required to obtain a reliable cortical and subcortical mapping. When excitability of the corticospinal neurons and of the corresponding efferent fibers might have been reduced by the previous treatment. Consequently, to evoke motor responses, a higher charge was required, which was obtained by increasing the number of pulses of the short train, associated in some cases also with an increase in the pulse duration. We preferred to follow this strategy along with inverting the polarity of the stimulation when needed, instead of increasing the current intensity, to reduce the risk of inducing stimulation-related intraoperative seizures.[3] At the end of the resection, when the tumor mass compression was removed, the excitability of M1 improved, as shown by the fact that the MEPs recorded from the cortical strip were elicited again by the standard To5 paradigm. Despite this, a transient paresis was observed in all patients, as usually occurs when functional boundaries are reached during resection. The efficacy of this approach is also confirmed by the very low rate of permanent morbidity. However, the underlying neuro physiological mechanism remains unclear.

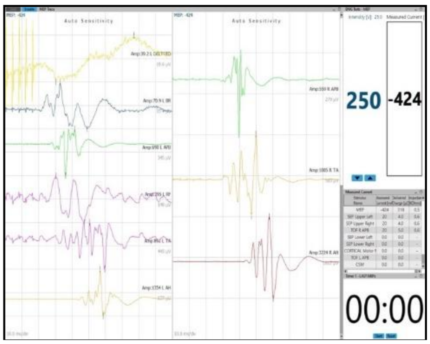

Fig 6. Baseline MEPs

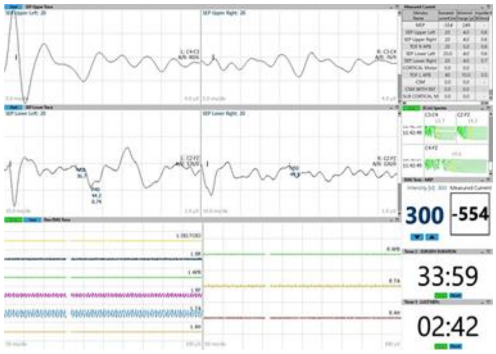

Fig 7. Baseline SSEPs

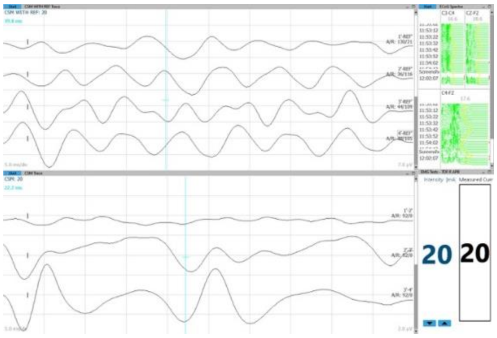

Fig 8. Central sulcus mapping - Phase reversal

Fig 9. Sub Cortical Mapping VE @ 15 mA : B/W 2-3 contact 1.5 cm

Fig 10. Cortical Stimulation +VE Hand area @ 5 mA

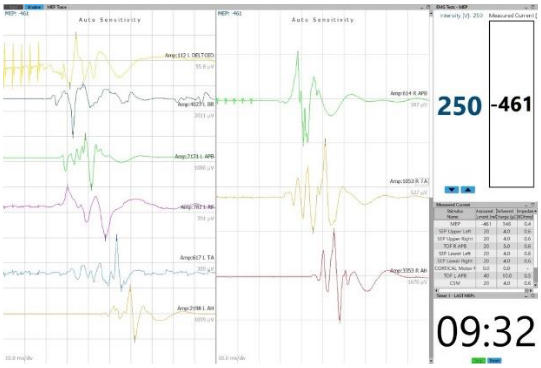

Fig 11. MEPs during Tumor Resection

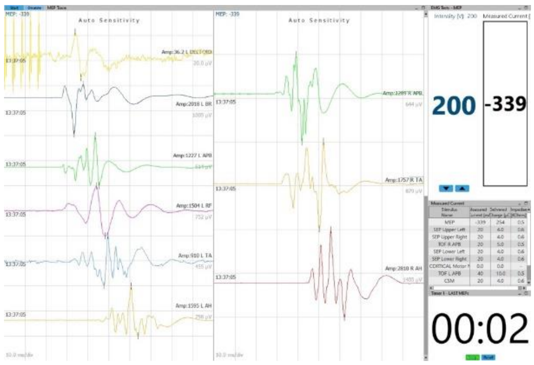

Fig 12. Final MEPs

Overall, these data indicate high versatility of the HF stimulation, which allows for reliable mapping in most clinical conditions. Cortically, the assessment of the threshold current is crucial in defining a reliable cortical mapping and identifying a safe cortical entry zone; subcortically, it is crucial to estimate the minimal distance between the functional motor fibers and the probe, which has to be adjusted according to clinical conditions. In this regard, the use of general anaesthesia is preferred, because it provides stable cortical excitability, crucial for the evaluation of quantitative parameters (i.e., MEP amplitude-current intensity), which can be quite variable in awake conditions. The intraoperative use of ECoG for detecting early cortical abnormalities further decreases the risk of inducing intraoperative seizures.

Limitations

This is a prospective study of only 6 patients and is limited by selection bias. The functional impact was evaluated using the MRC scale. The use of HF paradigms proposed in this paper requires some technical nuances, a sophisticated intraoperative machine, careful response interpretation by an in-house experienced neurophysiologist, and a neurophysiology-trained surgeon.

Conclusions

This study provides evidence that resection of tumors within M1 is feasible and safe when brain mapping is used. The reported experience was performed with HF stimulation, which is highly versatile. The key message is that the stimulation paradigm and probe must be appropriately adapted to clinical context, which then provides the best resection and functional results.

References

1. Bello L, Riva M, Fava E, Ferpozzi V, Castellano A, Raneri Rossi et al. F, et al: Tailoring neurophysiological strategies with clinical context enhances resection and safety and expands indications in gliomas involving motor pathways. Neuro Oncol 16:1110–1128, 2014
2. Buckner J, Giannini C, Eckel-Passow J, Lachance D, Parney I, Laack N, et al: Management of diffuse low-grade gliomas in adults—use of molecular diagnostics. Nat Rev Neurol 13:340–351, 2017
3. De Witt Hamer PC, Robles SG, Zwinderman AH, Duffau H, Berger MS: Impact of intraoperative stimulation brain mapping on glioma surgery outcome: a meta-analysis. J Clin Oncol 30:2559–2565, 2012
4. Duffau H, Mandonnet E: The "onco-functional balance" in surgery for diffuse low-grade glioma: integrating the extent of resection with quality of life. Acta Neurochir (Wien) 155:951–957, 2013
5. Han SJ, Morshed RA, Troncon I, Jordan KM, Henry RG, Hervey-Jumper SL, et al: Subcortical stimulation mapping of descending motor pathways for perirolandic gliomas: assessment of morbidity and functional outcome in 702 cases. J Neurosurg 131:201–208, 2019
6. Ius T, Angelini E, Thiebaut de Schotten M, Mandonnet E, Duffau H: Evidence for potentials and limitations of brain plasticity using an atlas of functional resectability of WHO grade II gliomas: towards a "minimal common brain." Neuroimage 56:992–1000, 2011
7. Magill ST, Han SJ, Li J, Berger MS: Resection of primary motor cortex tumors: feasibility and surgical outcomes. J Neurosurg 129:961–972, 2018
8. Noell S, Feigl GC, Naros G, Barking S, Tatagiba M, Ritz R: Experiences in surgery of primary malignant brain tumours in the primary sensori-motor cortex practical recommendations and results of a single institution. Clin Neurol Neurosurg 136:41–50, 2015

9. Obermueller T, Schaeffner M, Gerhardt J, Meyer B, Ringel F, Krieg SM: Risks of postoperative paresis in motor eloquently and non-eloquently located brain metastases. BMC Cancer 14:21, 2014
10. Penfield W, Boldrey E: Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain 60:389–443, 1937
11. Rossi et al. M, et al: Intraoperative electrical stimulation in awake craniotomy: methodological aspects of current practice. Neurosurg Focus 28(2):E7, 2010
12. Rossi M, Sani S, Nibali MC, Fornia L, Bello L, Byrne RW: Mapping in low-grade glioma surgery: low- and high frequency stimulation. Neurosurg Clin N Am 30:55–63, 2019
13. Sanai N, Berger MS: Glioma extent of resection and its impact on patient outcome. Neurosurgery 62:753–764, 264–266, 2008
14. Schucht P, Seidel K, Beck J, Murek M, Jilch A, Wiest R, et al: Intraoperative monopolar mapping during 5-ALA-guided resections of glioblastomas adjacent to motor eloquent areas: evaluation of resection rates and neurological outcome. Neurosurg Focus 37(6):E16, 2014
15. Seidel K, Beck J, Stieglitz L, Schucht P, Raabe A: Low threshold monopolar motor mapping for resection of primary motor cortex tumors. Neurosurgery 71 (1 Suppl Operative):104–115, 2012
16. Smith JS, Chang EF, Lamborn KR, Chang SM, Prados MD, Cha S, et al: Role of extent of resection in the long-term outcome of low-grade hemispheric gliomas. J Clin Oncol 26:1338–1345, 2008
17. Szelényi A, Bello L, Duffau H, Fava E, Feigl GC, Galanda J Neurosurg Volume 133 • September 2020 653 Unauthenticated | Downloaded 08/31/22 04:50 PM UTC
18. Szelényi A, Senft C, Jardan M, Forster MT, Franz K, Seifert V, et al: Intra-operative subcortical electrical stimulation: a comparison of two methods. Clin Neurophysiol 122:1470– 1475, 2011
19. van den Bent MJ, Wefel JS, Schiff D, Taphoorn MJB, Jaeckle K, Junck L, et al: Response assessment in neuro-oncology (a report of the RANO group): assessment of outcome in trials of diffuse low-grade gliomas. Lancet Oncol 12:583–593, 2011